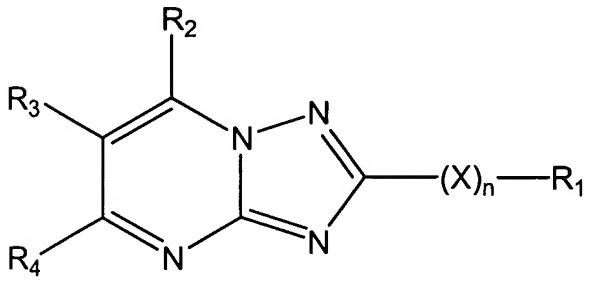
Amendments to the Claims:

This listing of clams will replace all prior versions, and listing, of claims in the application:

Listing of Claims:

1. (Currently amended): A combination in other than a human comprising a polypeptide comprising the modulating sequence of the erythropoietin receptor and a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

(I)



wherein:

X is of from 1 to 7 atoms other than hydrogen and is oxygen, sulfur bonded to 0 to 2 oxygen atoms, amino and alkyl substituted amino;

n is 0 or 1;

R_1 is hydrogen or an organic group of from 1 to 12 carbon atoms and from 0 to 6 heteroatoms, which are chalcogen, nitrogen, and halogen consisting of an aliphatic group of from 1 to 6 carbon atoms having from 0 to 2 sites of unsaturation, non-oxo-carbonyl and

the nitrogen and sulfur derivatives thereof, alicyclic having from 0 to 2 sites of unsaturation, aryl, heterocyclic and combinations thereof, where the cyclic structures may have from 1 to 2 rings;

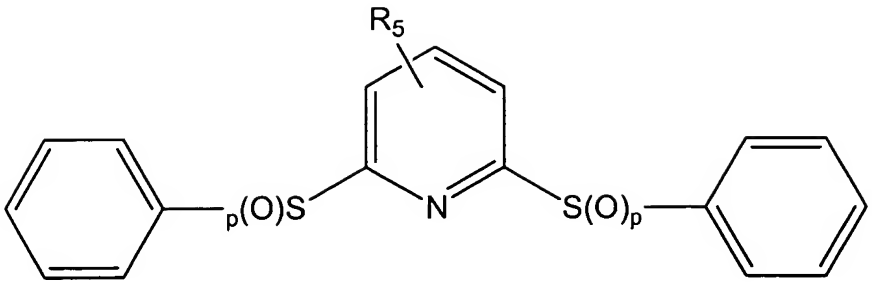
R_2 is hydrogen, a heterofunctionality having nitrogen and/or chalcogen bonded to annular carbon, a heterofunctionality having nitrogen and/or chalcogen bonded to annular carbon to which is substituted with an organic group of from 1 to 10 carbon atoms, aryl, alkaryl, aralkyl and aralkenyl of from 5 to 10 carbon atoms, aroyl of from 6 to 10 carbon atoms, or an organic group bonded through a carbon atom of from 1 to 12 carbon atoms having from 1 to 4, as described above for R_1;

R_3 is hydrogen or an organic group of from 1 to 10 carbon atoms and from 0 to 4 chalcogen and nitrogen heteroatoms;

R_4 is hydrogen or alkyl and substituted alkyl of from 1 to 6 carbon atoms, where the substituents are oxy, amino and halo;

with the proviso that R_3 and R4 can be taken together to form a ring with the annular atoms to which they are attached of from 4 to 10 annular atoms and forming from 1 to 2 rings, where the annular atoms are unsubstituted or substituted with halo, alkyl of from 1 to 3 carbon atoms, oxy of from 0 to 3 carbon atoms, thio of from 0 to 3 carbon atoms and amino of from 0 to 4 carbon atoms;

(2)

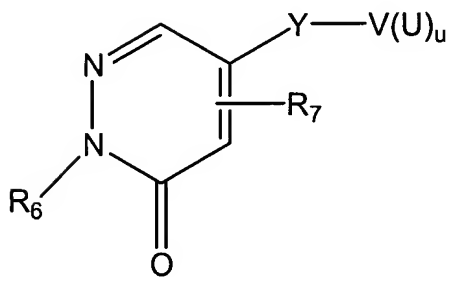


wherein:

p is 0, 1 or 2; and

R_5 is a group having from 1 to 3 atoms other than hydrogen and is oxy, thio, amino, nitro, cyano, and alkyl;

(3)



wherein:

Y is O, $S(O)_m$[[,]], wherein m is 0, 1 or 2, amino or CH_2;

R_6 is H or alkyl of from 1 – 3 carbon atoms;

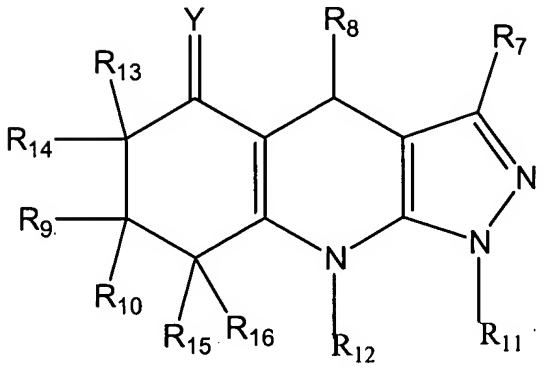
R_7 is hydrogen, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio amino, nitro, cyano, and alkyl;

V is an aryl group having 6 annular members comprising 0 to 2 nitrogen atoms and the remainder carbon atoms

U is a substituent group of from 0 to 5 atoms other than hydrogen, and is oxy, thio amino, nitro, cyano, halo, and alkyl; and

u is 0 to 3; or

(4) diazolohexahydroquinoline of the structure given below:



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wherein:

Y is oxygen, sulfur, NH, (alkyl of from 1 to 3 carbon atoms, H) or H_2

R_7 is hydrogen or an organic group of from 1 to 12 carbon atoms and 0 to 4 heteroatoms;

R_8 is hydrogen, an aliphatic group of from 1 to 6 carbon atoms or a heterocycle of from 5 to 6 annular members and from 1 to 2 heteroannular members that are oxygen, nitrogen or sulfur; and

R_9, R_{10}, R_{13}, R_{14}, R_{15} and R_{16} are the same or different and are hydrogen or an organic radical of from 1 to 12 carbon atoms or a heterosusbtituent of from 1 to 3 heteroatoms;

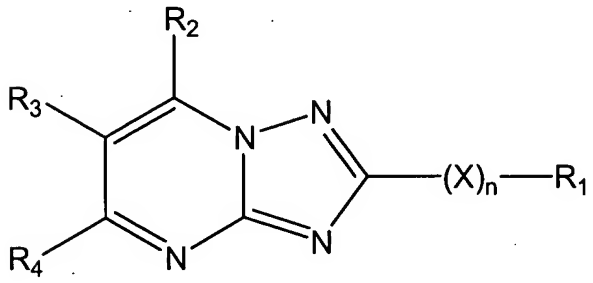
R_{11} and R_{12} are the same or different and are hydrogen or an organic group of from 1 to 12 carbon atoms.

2. (Original): A combination according to Claim 1, wherein said polypeptide and said non-peptide organic molecule are complexed at the modulating domain of EPO-R.

3. (Original): A combination according to Claim 2, wherein said polypeptide is EPO-R bound to a cellular membrane.

4. (Currently amended): A combination <u>in other than a human</u> comprising a polypeptide comprising the modulating domain sequence of the erythropoietin receptor and a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

(1)



wherein:

X is of from 1 to 3 atoms other than hydrogen and is oxygen, sulfur bonded to 0 to 2 oxygen atoms, amino and alkyl substituted amino;
n is 0 or 1;

R_1 is a lower alkyl group of 1 to 3 carbon atoms or an organic group having a six annular membered aromatic group having from 0 to 3 substituents, where the substituents are halo, lower alkyl of from 1 to 3 carbon atoms, nitro, trihalomethyl, and is either directly bonded to X or bonded through a linking group of from 1 to 4 carbon, nitrogen, or chalcogen atoms in the chain, being particularly carbon and nitrogen, and there being from 0 to 2 heteroatoms in the chain, where heteroatoms are bonded solely to carbon and hydrogen, or alpha-acetamidinyl having from 0 to 1 N-OH;

R_2 is hydrogen, amino of 0 to 3 carbon atoms, oxy of from 0 to 3 carbon atoms, a heterofunctionality having nitrogen or chalcogen bonded to annular carbon to which is substituted an organic group of from 1 to 10 carbon atoms and from 0 to 3 heteroatoms;

R_3 is hydrogen or an organic group of from 1 to 10 carbon atoms and from 0 to 4 chalcogen and nitrogen heteroatoms;

R_4 is hydrogen, alkyl or substituted alkyl of from 1 to 6 carbon atoms, where the substituents are oxy, amino and halo;

with the proviso that R_3 and R4 can be taken together to form a ring with the annular atoms to which they are attached of from 4 to 10 annular atoms and forming from 1 to 2 rings, where the annular atoms are unsubstituted or substituted with halo, alkyl of from 1 to 3 carbon atoms, oxy of from 0 to 3 carbon atoms, thio of from 0 to 3 carbon atoms and amino of from 0 to 4 carbon atoms.

5. (Original): A combination according to Claim 4, wherein R_3 is hydrogen or an organic group of from 1 to 8 carbon atoms and 0 to 4 chalcogen, nitrogen and halo heteroatoms.

6. (Original): A combination according to Claim 5, wherein R_3 is cyclopropylmethylamino.

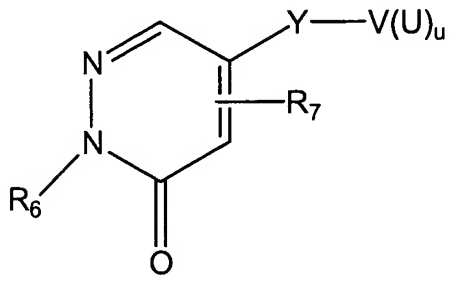
7. (Original): A combination according to Claim 5, wherein R_3 is H.

8. (Original): A combination according to Claim 4, wherein R_1 is a six annular membered aromatic group having from 0 to 3 substituents, where the substituents are halo, lower alkyl of from 1 to 3 carbon atoms, nitro, trihalomethyl, and is either directly bonded to X or bonded through a linking group of from 1 to 4 carbon, nitrogen, or chalcogen atoms in the chain.

9. (Original): A combination according to Claim 4, wherein R_4 is methyl.

10. (Original): A combination according to Claim 4, wherein R_4 is H.

11. (Currently amended) A combination <u>in other than a human</u> comprising a polypeptide comprising the modulating sequence of the erythropoietin receptor and a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:



(3)

wherein:

Y is O, $S(O)_m$[[,]], wherein m is 0, 1 or 2, amino or CH_2;

R_6 is H or alkyl of from 1 – 3 carbon atoms;

R_7 is hydrogen, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio amino, nitro, cyano, and alkyl;

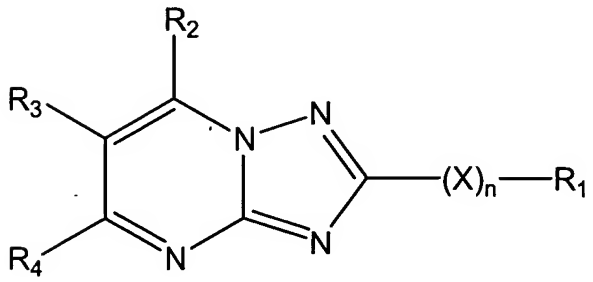
V is a phenyl group;

U is oxy, thio amino, nitro, cyano, halo, and alkyl and from 0 to 3 atoms other than hydrogen; and u is 0 to 3.

12. (Original): A combination according to Claim 11, wherein Y is SO_2, V is phenyl, R_7 is Cl and u is 0.

13. (Currently amended): A combination in other than a human comprising a polypeptide comprising the modulating domain sequence of the erythropoietin receptor and a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

(1)



wherein:

X is of from 1 to 3 atoms other than hydrogen and is oxygen, sulfur bonded to 0 to 2 oxygen atoms, amino and alkyl substituted amino;

n is 0 or 1;

R_1 is alkyl of from 1 to 3 carbon atoms, substituted phenyl having from 0 to 3 substituents that are CH_3, Cl, NO_2, and CF_3 and bonded directly to an annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms in the chain or N-hydroxyamidinyl;

R_2 is CH_3, NH_2, OH, and aroylamido of from 7 to 8 carbon atoms having from 0 to 2 substituents that are CH_3, Cl, NO_2, and CF_3;

R_3 is cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms, H or carboxy;

R_4 is H, lower alkyl of from 1 to 3 carbon atoms or alkoxymethyl of from 2 to 4 carbon atoms;

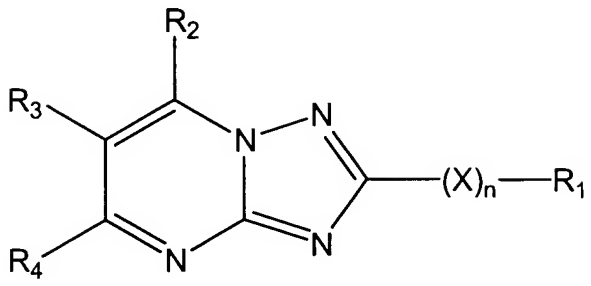
with the proviso that R_3 and R_4 may be taken together to define 1,2-dimethylene-alpha-halo, alpha-CH_3-halobenzene, where halo is F or Cl.

14-25. (Canceled)

26. (Currently amended): A ~~compound according to Claim 13~~ pharmaceutical composition comprising:

in a pharmacologically effective amount for modulating EPO-R activity, a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

(1)



wherein:

X is of from 1 to 3 atoms other than hydrogen and is oxygen, sulfur bonded to 0 to 2 oxygen atoms, amino and alkyl substituted amino;
n is 0 or 1;

R_1 is alkyl of from 1 to 3 carbon atoms, substituted phenyl having from 0 to 3 substituents that are CH_3, Cl, NO_2, and CF_3 and bonded directly to an annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms in the chain or N-hydroxyamidinyl;

R_2 is CH_3, NH_2, OH, and aroylamido of from 7 to 8 carbon atoms having from 0 to 2 substituents that are CH_3, Cl, NO_2, and CF_3;

R_3 is cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms, H or carboxy;

R_4 is H, lower alkyl of from 1 to 3 carbon atoms or alkoxymethyl of from 2 to 4 carbon atoms;

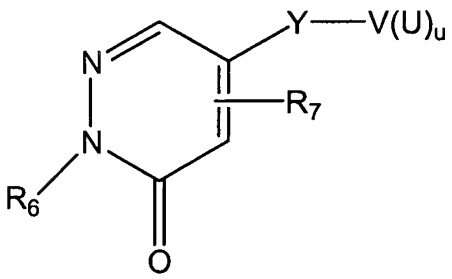
with the proviso that R_3 and R_4 may be taken together to define 1,2-dimethylene-alpha-halo, alpha-CH_3-halobenzene, where halo is F or Cl

and a pharmaceutically acceptable vehicle.

27. (Currently amended): A ~~compound according to Claim 11~~ pharmaceutical composition comprising:

in a pharmacologically effective amount for modulating EPO-R activity, a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

(3)



wherein:

Y is O, $S(O)_m$, wherein m is 0, 1 or 2, amino or CH_2;

R_6 is H or alkyl of from 1 – 3 carbon atoms;

R_7 is hydrogen, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio amino, nitro, cyano, and alkyl;

V is a phenyl group;

U is oxy, thio amino, nitro, cyano, halo, and alkyl and from 0 to 3 atoms other than hydrogen; and u is 0 to 3, and a pharmaceutically acceptable vehicle.

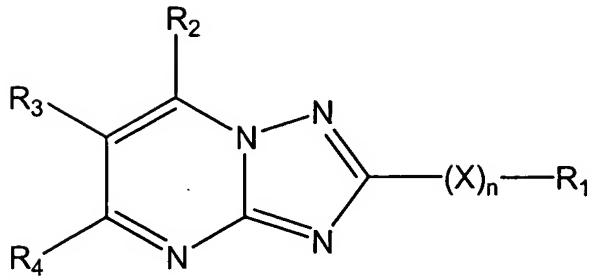
28. (Withdrawn): A method of determining the binding affinity of a test compound to the modulating domain of EPO-R, said method comprising:

adding said test compound to a combination according to Claim 1 and determining the amount of complex of said combination in the presence of said test compound as compared to the absence of said test compound.

29. (Withdrawn): A method of inducing a physiological response of EPO-R in a host, said method comprising:

administering to said host a physiologically effective amount of a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

(1)



wherein:

X is of from 1 to 3 atoms other than hydrogen and is oxygen, sulfur bonded to 0 to 2 oxygen atoms, amino and alkyl substituted amino;
n is 0 or 1;

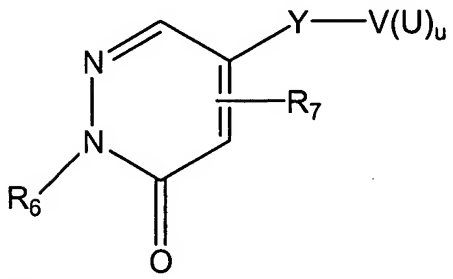
R_1 is alkyl of from 1 to 3 carbon atoms, substituted phenyl having from 0 to 3 substituents that are CH_3, Cl, NO_2, and CF_3 and bonded directly to an annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms in the chain, N-hydroxyamidinyl;

R_2 is CH_3, NH_2, OH, and aroylamido of from 7 to 8 carbon atoms having from 0 to 2 substituents that are CH_3, Cl, NO_2, and CF_3;

R_3 is cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms, H or carboxy;

R_4 is H, lower alkyl of from 1 to 3 carbon atoms or alkoxymethyl of from 2 to 4 carbon atoms;

with the proviso that R_3 and R_4 may be taken together to define 1,2-dimethylene-alpha-halo, alpha-CH_3-halobenzene, where halo is F or Cl; or



(2)

wherein:

X is of from 1 to 3 atoms other than hydrogen and is oxygen, sulfur bonded to 0 to 2 oxygen atoms, amino and alkyl substituted amino;

n is 0 or 1;

Y is O, $S(O)_m$, wherein m is 0, 1 or 2, amino or CH_2;

R_6 is H or alkyl of from 1 – 3 carbon atoms;

R_7 is hydrogen, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio amino, nitro, cyano, and alkyl;

V is a phenyl group;

U is oxy, thio amino, nitro, cyano, halo, and alkyl and from 0 to 3 atoms other than hydrogen; and u is 0 to 3.

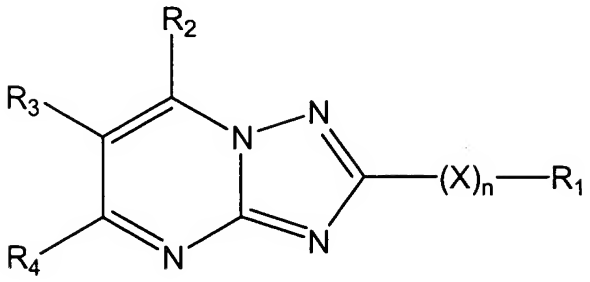
30. (Withdrawn): A method according to Claim 29, wherein said non-peptide organic molecule is of formula 1.

31. (Withdrawn): A method according to Claim 30, wherein X is amino, R_2 is o-methyl, p-chlorophenyl-1, R_2 is H, R_3 is cyclopropylmethylamino and R_4 is methyl.

32. (Withdrawn): A method of modulating the response to a stimulus of hematopoietic or neuronal cells influenced by the binding of EPO to EPO-R, said method comprising:

contacting said cells with an effective amount to modulate said response of a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

(1)



wherein:

R_1 is alkyl of from 1 to 3 carbon atoms, substituted phenyl having from 0 to 3 substituents that are CH_3, Cl, NO_2, and CF_3 and bonded directly to an annular carbon atom or through a linking group of from 1 to 3 carbon and nitrogen atoms in the chain, N-hydroxyamidinyl;

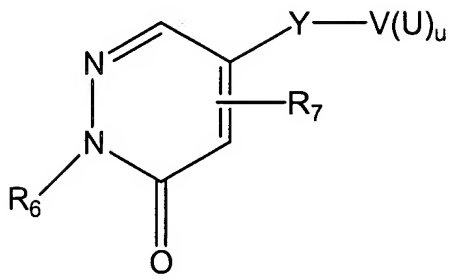
R_2 is CH_3, NH_2, OH, and aroylamido of from 7 to 8 carbon atoms having from 0 to 2 substituents that are CH_3, Cl, NO_2, and CF_3;

R_3 is cycloalkylalkyl of from 4 to 8 carbon atoms, having from 3 to 4 annular atoms, H or carboxy;

R_4 is H, lower alkyl of from 1 to 3 carbon atoms or alkoxymethyl of from 2 to 4 carbon atoms;

with the proviso that R_3 and R_4 may be taken together to define 1,2-dimethylene-alpha-halo, alpha-CH_3-halobenzene, where halo is F or Cl; or

(3)



wherein:

Y is O, $S(O)_m$, wherein m is 0, 1 or 2, amino or CH_2;

R_6 is H or alkyl of from 1 – 3 carbon atoms;

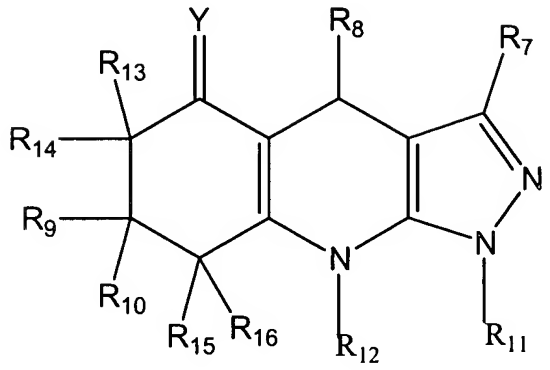
R_7 is hydrogen, or a group of from 0 to 3 atoms other than hydrogen, and is oxy, thio amino, nitro, cyano, and alkyl;

V is a phenyl group; and

U is oxy, thio amino, nitro, cyano, halo, and alkyl and from 0 to 3 atoms other than hydrogen; and u is 0 to 3.

33. (Currently amended): A combination comprising <u>in other than a human</u> a polypeptide comprising the modulating sequence of the erythropoietin receptor and a non-peptide organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:

diazolohexahydroquinoline



wherein:

Y is oxygen, sulfur, NH, (alkyl of from 1 to 3 carbon atoms, H) or H_2

R_7 is hydrogen or an organic group of from 1 to 12 carbon atoms and 0 to 4 heteroatoms;

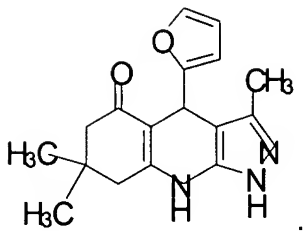
R_8 is hydrogen, an aliphatic group of from 1 to 6 carbon atoms or a heterocycle of from 5 to 6 annular members and from 1 to 2 heteroannular members that are oxygen, nitrogen or sulfur; and

R_9, R_{10}, R_{13}, R_{14}, R_{15} and R_{16} are the same or different and are hydrogen or an organic radical of from 1 to 12 carbon atoms or a ~~heterosusbtituent~~ heterosubstituent of from 1 to 3 heteroatoms;

R_{11} and R_{12} are the same or different and are hydrogen or an organic group of from 1 to 12 carbon atoms.

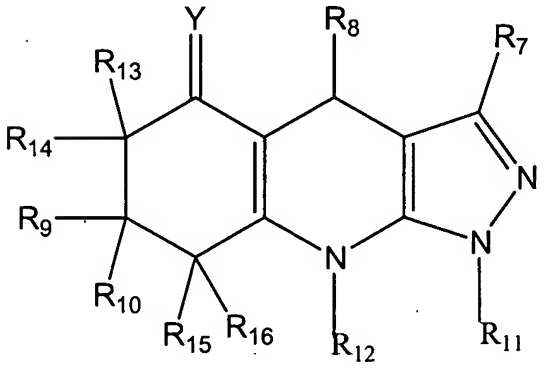
34. (Canceled)

35. (Previously presented): A combination according to claim 33, wherein said diazolohexahydroquinoline is of the formula:



36. (New): A pharmaceutical composition comprising:

in a pharmacologically effective amount for modulating EPO-R activity, a non-peptide diazolohexahydroquinoline organic molecule of from 12 to 36 atoms other than hydrogen, from 9 to 20 carbon atoms, and from 4 to 12 of the heteroatoms chalcogen, nitrogen, halogen, and metal ion of Groups I and II of the periodic chart, and of the formula:



wherein:

Y is oxygen, sulfur, NH, (alkyl of from 1 to 3 carbon atoms, H) or H_2

R_7 is hydrogen or an organic group of from 1 to 12 carbon atoms and 0 to 4 heteroatoms;

R_8 is hydrogen, an aliphatic group of from 1 to 6 carbon atoms or a heterocycle of from 5 to 6 annular members and from 1 to 2 heteroannular members that are oxygen, nitrogen or sulfur; and

R_9, R_{10}, R_{13}, R_{14}, R_{15} and R_{16} are the same or different and are hydrogen or an organic radical of from 1 to 12 carbon atoms or a heterosubstituent of from 1 to 3 heteroatoms;

R_{11} and R_{12} are the same or different and are hydrogen or an organic group of from 1 to 12 carbon atoms, and a pharmaceutically acceptable vehicle.

37. (New): A pharmaceutical composition according to claim 36, wherein said diazolohexahydroquinoline is of the formula: